DOI:
10.1002/mrm.26757

Document Version
Peer reviewed version

Fully-Integrated 3D High-Resolution Multi-Contrast Abdominal PET-MR with High Scan Efficiency

Christoph Kolbitsch[1,2], Radhouene Neji[3], Matthias Fenchel[4], Andrew Mallia[2], Paul Marsden[2], Tobias Schaeffter[1,2]

[1]Physikalisch-Technische Bundesanstalt, Medical Physics and Metrological Information Technologies, Berlin, Germany

[2]King's College London, Division of Imaging Sciences and Biomedical Engineering, London, UK

[3]MR Research Collaborations, Siemens Healthcare, Frimley, UK

[4]MR Oncology Application Development, Siemens Healthcare, Erlangen, Germany

Short running head:

Fully-Integrated 3D Abdominal PET-MR

Corresponding author:

Christoph Kolbitsch, Physikalisch-Technische Bundesanstalt (PTB), Abbestraße 2-12, 10587 Berlin, Germany, E-mail: christoph.kolbitsch@ptb.de

Full paper

Word count: 5550

Abstract

Purpose: To provide 3D multi-contrast anatomical MR with high isotropic resolution and metabolic PET images using a respiratory motion-compensated simultaneous PET-MR examination with high scan efficiency.

Theory and Methods: Standard abdominal PET-MR examinations combine MR data obtained during multiple breathholds with free-breathing PET acquisitions, limiting the achievable image resolution and potentially causing misalignment errors between breathhold and free-breathing data. Here a 3D free-breathing PET-MR acquisition is presented, yielding T1- and T2-weighted MR images with an isotropic resolution of 1.5mm^3. In addition, non-rigid respiratory motion information and respiratory-resolved attenuation correction maps are obtained without an increase in scan time. Motion information is utilized in motion-compensated image reconstructions to improve MR and PET image quality while shortening scan times.

Results: The proposed approach was evaluated in eleven oncology patients and provided respiratory motion information with an accuracy of 1.3±0.1mm. Sharpness of anatomical features was increased by 19±13% compared to the uncorrected MR images in a 54±26% shorter scan time than a gated MR acquisition. MR-based motion information improved uptake values (75±94%) and resolution (16±27%) of simultaneously acquired PET images.

Conclusion: The proposed method provides motion-compensated 3D high quality MR and PET images in a comprehensive and highly efficient examination.

Keywords: simultaneous PET-MR, respiratory motion compensation, abdominal imaging, golden radial phase encoding

INTRODUCTION

Simultaneous positron emission tomography (PET)-MR enables the acquisition of highly sensitive PET and versatile high-resolution MR data during a single examination (1–3). Simultaneous PET-MR is a promising new technology, especially for oncological applications which require high soft-tissue contrast, such as detection of liver metastasis or assessment of renal masses and for pediatric oncology (4–7). Anatomical MR data with different contrasts such as T1-weighted (T1w) gradient echo (GRE) or T2-weighted (T2w) spin echo (SE) images provide complimentary diagnostic information to metabolic PET and lead to a better lesion detection and characterization especially for small pathologies compared to PET-Computed Tomography (CT) (4).

Respiratory motion in the abdomen can lead to organ displacements of up to 10 mm and can strongly impair MR and PET image quality (8–10). For abdominal PET-MR scans the PET acquisition is commonly carried out during free-breathing (Fig. 1) and takes between 5 to 10 min. Physiological motion impairs PET image quality in two ways. The movement of structures emitting PET signals leads to a blurring of the final image. In addition, motion can cause misalignment errors between emission and attenuation correction (AC) information. Retrospective respiratory gating can be used to reduce motion blurring and improve the visualization of small uptake structures. This, however, also reduces the already low signal-to-noise-ratio (SNR) of PET images (11).

Several in-vivo PET-MR approaches have been presented to use MR-derived motion information to compensate for breathing artefacts and improve PET image quality (12–18). Although 3D motion correction is carried out, motion information for all of these methods is obtained with poor slice resolution between 4.5 and 10 mm. In addition, all of these techniques require additional scan time (between 1 and 10 min) just for motion estimation, which limits the overall efficiency of these approaches.

The reconstruction of quantitative PET images requires additional AC images which are used to compensated for the varying density of different tissue types. The AC information is obtained from a MR Dixon scan which is commonly acquired during a single breathhold (19). This can result in misalignment errors between breathhold AC map and free-breathing PET data, also referred to as attenuation-emission mismatch (11,20,21). It can lead to a complete signal loss in large areas of PET images often seen around the hemidiaphragm (“banana-artefact”) and is well known from PET-CT. Furthermore, any artefacts in the MR-based AC map, due to an incomplete breathhold for example, can also cause image artefacts and, importantly, incorrect PET quantification (20).

The anatomical T1w and T2w MR images are acquired during multiple breathholds or using respiratory triggering to minimize respiratory motion artefacts (21). Breathholding strongly limits the achievable image resolution (e.g. 5mm slice thickness) and field-of-view (FOV) (e.g. 20 – 30 slices). T2w scans are therefore often repeated in different orientations to allow for an accurate diagnosis independent of the slice orientation. Respiratory triggering has been proposed to overcome these limitations but requires long scan times. Even for a slice thickness of 5 mm, respiratory-triggered TSE acquisitions can take 6 -7 min because the TR is adapted to the respiratory cycle and can be more than 5500 ms (22). Respiratory-triggered TSE images with high isotropic resolution would therefore not be possible within the time frame of approximately 10 min for one station (i.e. axial FOV of 26 cm) of a PET acquisition. In addition, the final image quality and scan time (i.e. scan efficiency) is strongly dependent on patient specific factors, such as patients' breathing pattern or the patients' compliance and ability to hold their breath.

For standard PET-MR examination, images are acquired in different respiratory motion states (e.g. free-breathing for PET, multiple breathholds for T1w and T2w) and images are therefore not necessarily spatially aligned despite the truly simultaneous data acquisition. In addition, MR scans are highly inefficient, utilizing only a small part of the total scan time for image acquisition and thus limiting the available FOV and image resolution.

Here we propose a novel approach providing 3D Dixon T1w and T2w MR data with high isotropic-resolution covering the entire abdomen. All data is acquired during free-breathing and motion-compensated MR and PET image reconstructions (MCIR) are carried out to minimize motion artefacts and ensure a high scan efficiency for MR and PET. All images are motion-corrected to the same end-expiratory motion state using a global motion surrogate making them fully spatially aligned. The required motion information is obtained directly from the diagnostic MR scans without an increase in scan time. Respiratory-resolved AC information is calculated from the T1w diagnostic scan to ensure AC map and PET emission data are in the same motion state minimizing any attenuation-emission mismatch errors. No additional breathhold AC scan is required.

METHODS

A 3D T1w triple-echo GRE acquisition and a 3D T2w fat-suppressed single-shot TSE acquisition are obtained with an isotropic resolution of 1.5 mm^3 covering a FOV of 288 x 519 x 519 mm^3. Both scans are carried out during free-breathing using a GRPE sampling scheme and PET list-mode data are acquired simultaneously. In an initial motion estimation step, T1w and T2w raw data are binned into respiratory

motion states using a respiratory belt as a global motion surrogate with high temporal resolution. 3D images at different stages of the breathing cycle are reconstructed and motion-vector fields (MVF_{GRE} and $MVF_{TSE,}$ respectively) are obtained, which describe the motion of each pixel during the respiratory cycle. In a second motion compensation step, MVF are utilized to minimize respiratory artefacts in a motion-compensated image reconstruction (MCIR) of the T1w and T2w data by transforming all acquired data to the same respiratory motion state (23). MCIR multi-echo GRE data are then separated based on their fat and water content to provide anatomical T1w images with excellent fat suppression and dynamic respiratory-resolved AC information (AC_{Dyn}) for quantitative PET reconstructions. In a final step, a motion-compensated PET image is obtained using MVF and AC_{Dyn} (24,25).

MR Data Acquisition

MR data acquisition is carried out using GRPE (26). This sampling scheme combines Cartesian frequency encoding with non-Cartesian phase encoding (Fig. 2). The individual phase encoding steps are obtained along radial lines. The angle between two successive GRPE lines is the golden angle (111.25°). This leads to a homogenous covering of the 2D phase encoding plane over time which provides important flexibility for image reconstruction. High quality 3D images can be obtained by combining all the acquired data (providing e.g. anatomical information) or 3D dynamic images can be reconstructed by separating the data into different motion bins (providing e.g. respiratory resolved images) (8).

The undersampling properties of GRPE are improved by interleaving the sampling positions along the radial phase-encoding direction for neighboring GRPE lines (27).

MR Data Correction

The multi-echo GRE data is obtained with a bipolar readout gradient which requires correction of phase errors between odd and even echoes caused by hardware limitations (28). For GRPE a central readout (i.e. ky = 0 and kz = 0) is obtained for each GRPE line. This provides sufficient data to carry out the phase correction and no additional calibration data has to be acquired.

Partial Fourier acquisition is used along the readout direction for GRE and along the radial phase-encoding direction for TSE. A homodyne reconstruction approach is used to compensate for this partial sampling of k-space by applying a weighting function along each partially sampled k-space direction to compensate for the missing k-space data and minimize blurring effects (29).

Motion Binning

A respiratory belt is used as a global respiratory surrogate with high temporal resolution. This ensures that MCIR MR and PET images are motion-corrected to the same global motion state and are fully spatially aligned. The respiratory belt provides a qualitative motion signal which is used for data binning and the MVF obtained from the binned images then yield quantitative motion information (i.e. motion displacement in millimeters). The acquired T1w and T2w MR data are binned into N_{Resp} respiratory motion states based on the amplitude of the respiratory belt signal such that each bin contains the same amount of acquired MR data. This leads to a comparable image quality for each motion state providing a more robust image registration. The binning is carried out using a soft-gating approach for each motion state (30).

MR Image Reconstruction and Motion Estimation

A non-Cartesian iterative sensitivity encoding (SENSE) reconstruction scheme is used to reconstruct a 3D image $\widehat{I_r}$ for each respiratory motion state r from the acquired k-space data K by solving:

$$\hat{I}_r = \arg\min(\|EI_r - K_r\|_2^2 + \lambda\|\nabla I_r\|_1 + \lambda_r\|\nabla_r I_r\|_1) \quad [1]$$

as proposed by Cruz et al. (31). The encoding operator E describes the weighting of the image by the coil sensitivities, Fourier transforming the image data to k-space and gridding from Cartesian to non-Cartesian k-space. ∇ and ∇_r describe image gradients along 3D spatial and 1D respiratory resolved (i.e. temporal) directions. Spatial ($\|\nabla I_r\|_1$) and temporal ($\|\nabla_r I_r\|_1$) total variation constraints are used to utilize data redundancy and ensure high image quality. The tradeoff between spatial and temporal regularization and data consistency is set by the parameters λ and λ_r.

Non-rigid motion is estimated between an end-expiratory reference motion state and all other respiratory phases (32). MFV are determined using cubic b-splines and an objective function which combines a similarity measure based on pixel-wise mutual information and a bending energy penalty term. The image registration yields two different displacement fields, i.e. N_{resp} MFV for the T1w and N_{resp} MFV for the T2w scan describing the movement of each pixel due to breathing.

MR Motion-Compensated Image Reconstruction

The obtained MFV are utilized in a MCIR with spatial total variation regularization to obtain the final motion-compensated 3D MR images $\hat{I}$ similar to equation [1] (31):

$$\hat{I} = \arg\min(\|EI - K\|_2^2 + \lambda\|\nabla I\|_1) \quad [2]$$

The main difference here is, that the encoding operator E now also incorporates respiratory motion information to obtain a motion artefact free image (23). Motion-compensated multi-echo GRE images are then separated into fat and water images to calculate AC maps required for the PET reconstruction (33).

Calculation of Attenuation Map

In order to obtain quantitative PET images, the varying density of different tissue types need to be compensated for using AC maps. The reconstructed fat and water MCIR images are classified into different tissue types and each tissue type is assigned a constant attenuation value: air 0 cm^{-1}, lung tissue 0.02 cm^{-1}, soft tissue 0.1 cm^{-1} and fat tissue 0.09 cm^{-1}. MVF are used to transform the end-expiratory AC information to the different breathing phases providing a dynamic respiratory motion-resolved AC map (AC_{Dyn}) which accurately describes the different tissue densities for each of the motion states of the free-breathing PET acquisition.

PET Data Acquisition and Image Reconstruction

PET list-mode data is acquired simultaneously during T1w and T2w scans. List-mode data is binned into 2 x N_{Resp} motion states – N_{Resp} for data acquired during the T1w scan and N_{Resp} for data obtained during the T2w scan – in the same way as the binning of the respective MR data was carried out. The binned list-mode data, the two sets of MVF and the respiratory resolved AC map are then utilised in an iterative MCIR ordered subsets expectation maximization PET reconstruction to transform the acquired data to a reference motion state in each iteration (34). A detailed description of the reconstruction algorithm can be found in (35).

Random and scatter events are corrected separately for each motion state (36,37). The random events are estimated from single events. For the scatter correction, attenuation corrected PET images are reconstructed and single scatter events are estimated from these emission images. The single scatter data is then scaled using a tail-fit method. The regions for the estimation of the tail-fit scaling are selected based on thresholding the AC maps. This process is repeated multiple times by correcting the PET sinograms with the currently estimated scatter events and iteratively improving the scatter calculation.

Patient Population

Eleven patients (10 male and 1 female, 61 $\pm$ 11 y, 77 $\pm$ 16 kg) were included in this study who had been referred to our hospital for staging or restaging of malignant diseases using PET-CT. Patients' diagnosis

included metastatic pancreatic cancer, lymphoma, sarcoidosis, melanoma, lung carcinoma, pleural thickening, metastatic neuroendocrine tumors and esophageal cancer. For the PET-CT scan, ten patients were injection with 337 $\pm$ 25 MBq of ^{18}F-FDG and one patient (metastatic neuroendocrine tumors) received an injection of 169.5 MBq ^{68}Ga-DOTATATE. Patients gave written informed consent to take part in the study and to undergo a PET-MR scan after the original PET-CT scan without any additional injection of a radionuclide tracer. PET-MR imaging was carried out 153 $\pm$ 23 min after initial injection of the PET tracer. The study was approved by our National Research Ethics Service Committee (reference number: 15/LO/0978).

Experiments

A triple-echo GRE Dixon GRPE and a TSE GRPE prototype sequence were implemented on a Siemens Biograph mMR 3T scanner and patients were imaged with a FOV of 288 x 519 x 519 mm^3 and an isotropic resolution of 1.5 x 1.5 x 1.5 mm^3. A summary of the acquisition parameters is given in Tab. 1. Both T1w and T2w scans used a non-selective RF excitation pulse and data acquisition was carried out using phased array coils. The number of elements was selected automatically based on the size of the patient and the location of the FOV. For all patients 8 respiratory motion states were defined (N_{Resp} = 8).

All MR images were reconstructed offline using Matlab (The MathWorks, Inc., Natich, MA, USA). The required coil sensitivity maps were calculated from the data itself. For comparison purposes MR images were also reconstructed without motion compensation using a standard non-Cartesian iterative SENSE reconstruction approach (38).

PET image reconstruction was carried out using Software for Tomographic Image Reconstruction (STIR) (39). An iterative three-dimensional ordered subsets expectation maximization algorithm with 23 subsets and three full iterations and 4 mm isotropic 3D Gaussian post-filtering was used. The images were reconstructed to a matrix size of 344 x 344 x 127 with a spatial resolution of 2.1 x 2.1 x 2.0 mm^3.

To evaluate the proposed approach, a standard Cartesian MRAC scan (AC_{Cart}) was carried out during a single breathhold and PET images using AC_{Cart} were reconstructed without motion compensation. In addition, respiratory gated PET images were also reconstructed using AC_{Cart} and restricting image reconstruction to 30% of the total data based on the amplitude of the respiratory belt.

Evaluation of Respiratory Belt Signal

The GRPE trajectory obtains a central k-space (ky = 0 and kz = 0) projection for each GRPE line. These projections are 1D projections of the FOV along the foot-head direction and can be used to obtain a self-navigator signal (31,40). The respiratory belt signal was compared to the corresponding self-navigator signal obtained from the multi-echo GRE Dixon GRPE acquisition to verify the accuracy of the belt and ensure it was well positioned. The quality was assessed by calculating the correlation-coefficient between the two surrogate signals.

Accuracy of Motion Estimation

The amplitude of respiratory motion and the accuracy of the obtained MVF was determined using anatomical landmark points (LM_i). Positions of LM_i were manually selected at anatomically well-defined locations in each of the respiratory phases. The maximum displacement (D_{max}) of LM_i due to respiratory motion was calculated as

$$D_{max} = \max_j \left| LM_j - LM_{i=1} \right|$$

The accuracy of MVF was determined by calculating the target registration error (TRE) between LM_i and the position of the landmark points predicted by MVF. Applying MVF_j to $LM_{i=1}$ (i.e. the position of the landmarks in end-expiration) yields the prediction of the landmark position in the j^{th} motion state. TRE is then determined as the distance between LM_j and $MVF_j(LM_{i=1})$:

$$TRE = \frac{1}{N} \sum_{j=1}^{N} \left| LM_j - MVF_j(LM_{i=1}) \right|$$

For this study two landmark points were selected in the liver and three in the left and right kidney, respectively.

MR Image Quality Assessment

The image quality of the uncorrected and motion-compensated MR images was assessed using the feature sharpness (FS) calculated along the right hemidiaphragm and along the lower renal cortex of the right and left kidney average over multiple coronal slices.

FS is derived from coronary artery imaging where the sharpness of the coronary arteries has become a widely used image quality parameter (41–43). Applied to the liver it has been used previously to assess improvements in image quality using motion-compensation techniques (31). It provides an automatic measure which is not dependent on human observers and is well-suited to assess 3D data sets.

For FS a Deriche edge detection filter is applied to the image and the maximum value in the obtained edge image ($Edge_{Max}$) is obtained. FS is determined as the ratio between $Edge_{Max}$ and the maximum value along the edge in the original image. FS lies within [0,1], with 1 representing an ideal edge, i.e. a Heaviside step function.

The standard approach to minimize respiratory motion artefacts for abdominal MRI with high isotropic resolution would be to use respiratory gating or triggering. The scan efficiency of such an approach was determined by simulating a respiratory-gated MR acquisition with a 5 mm gating window using a pencil beam navigator placed on the right hemidiaphragm. The simulated navigator signal was calculated using the displacement information of the MVF.

Evaluation of AC Maps

The Dice similarity coefficient was calculated between the tissue classification of breathhold AC scans and the classification obtained from the end-expiratory phase of AC_{Dyn} for each tissue type (44). MR field inhomogeneities at the edge of the FOV can cause image distortions leading to artefacts mainly along patients' arms. The appearance of these artefacts varies between different MR scans and therefore the Dice coefficient was only evaluated for the torso.

In order to assess how well the PET and MR images are spatially aligned, overlays of MR and PET images were scored by a clinical reviewer with expertise in PET-MR imaging who was blinded to the reconstruction method. The score was "minor", "moderate" and "mayor" misalignment errors. The scoring was carried out on central coronal slices and compared the overlay of MCIR T2w MR with uncorrected and MCIR PET images in a randomized way.

PET Image Quality Assessment

In each patient three small features with high uptake (e.g. tumors in the liver or nodules in the kidney) were manually selected to assess the improvement in PET image quality using MCIR compared to the uncorrected and 30%-gated PET images. The full-width-at-half-maximum (FWHM) was determined in foot-head direction (the dominating respiratory motion direction) by fitting a Gaussian curve to the measured profiles. In addition, the SNR of these small features was calculated as the difference between the maximum standardized uptake value and the mean value of the surrounding tissue relative to the standard deviation measured in a homogenous area of surrounding tissue.

Statistical significance of any improvement in image quality was assessed with a paired student t-test considering a p value smaller than 0.05 as statistically significant. A linear regression analysis was carried out to evaluate if the accuracy of the MVF (i.e. TRE) is dependent on the respiratory motion amplitude.

RESULTS

Simultaneous PET-MR scans were successfully completed in all patients. The TR of the T2w TSE scan had to be adapted for some larger patients (patient weight ranged from 48.2 to 117 kg) due to specific absorption rate (SAR) limitations, leading to an average scan time of 11.31 $\pm$ 1.34 min for the entire PET-MR examination.

Evaluation of Respiratory Belt Signal

The average correlation coefficient between the self-navigator signal obtained from the multi-echo GRE Dixon GRPE sequence and the respiratory belt was 0.7 $\pm$ 0.13.

Accuracy of Motion Estimation

Figure 3 shows the selected landmark points for one patient and TRE over all patients and scans. The maximum displacement (D_{max}) due to breathing varied strongly between subjects ranging from 3.3 to 10.6 mm (6.5 $\pm$ 1.6 mm). The obtained motion fields reduced the average maximum displacement over all 1408 manually selected landmark positions to a target registration error of 1.3 $\pm$ 0.1 mm. There was no statistically significant difference between the T1w and T2w scans for D_{max} ($p>0.2$). A linear regression analysis of TRE as a function of D_{max} led to a $R^2 > 0.2$, indicating that TRE did not depend on the respiratory motion amplitude and accurate motion information both for patients with deep and with shallow breathing patterns.

Improvement in MR Image Quality

T1w and T2w images with and without MCIR are displayed in Fig 4 for different patients. MCIR minimizes respiratory motion artefacts and leads to a better depiction of both anatomy and pathologies. A hemorrhagic cyst, which appeared bright on T1w images, was not visible without MCIR due to motion blurring (Fig. 4a). Small tumors in the liver were impaired by respiratory motion and their visibility was improved using MCIR (Fig. 4b). Even large vessels in the kidney were strongly blurred due to breathing and could be restored using MCIR (Fig. 4c). Patients shown in Fig. 4d and 4e both have cysts in the kidneys,

which appear hyper-intense on the T2w images. MCIR strongly improves the visualization of these pathologies and also of the surrounding kidney structures. In Fig. 4f the urethra is hardly visible in the uncorrected images but is clearly defined in the MCIR images. In addition, respiratory motion impaired the interface between spleen and lung which was completely restored using MCIR. The hypo-intense liver vessels are also better depicted in the MCIR images than the uncorrected MR images.

FS was increased by 19±14% ($p<0.0001$) for the T1w and 19±11% ($p<0.0001$) for the T2w MCIR images compared to the uncorrected images (Fig. 5). The increase in FS was larger for the hemidiaphragm due to the larger motion amplitude compared to the kidneys.

The proposed approach utilizes all the acquired data (100% scan efficiency) and compensates for respiratory motion using MCIR. Acquiring T1w and T2w images with high isotropic resolution using respiratory gating would have led to scan efficiencies as low as 37% (67 $\pm$ 12%) and scan times of more than 25 min (18 $\pm$ 4min).

Accuracy of AC Maps

Dixon-based fat-water separation and tissue segmentation was successfully carried out for all patients leading to Dice coefficients of 1.0 $\pm$ 0.001 for background pixels, 0.68 $\pm$ 0.091 for air inside the body, 0.72 $\pm$ 0.073 for fat and 0.81 $\pm$ 0.034 for soft tissue (Fig. 6). The standard breathhold MRAC scans showed artefacts in the lungs in some patients and poor lung-liver delineation due to incomplete breathhold, which did not occur in the proposed MCIR free-breathing scans (Fig. 6). These artefacts led to overcorrection of PET uptake potentially mimicking lung tumors. Figure 7b shows an example of an AC map acquired during a very deep breathhold. This breathing state did not match the free-breathing PET acquisition leading to large signal dropouts at the top of the liver and spleen which were falsely corrected with lung AC values (“banana-artefact”). For the standard breathhold AC approach major misalignment errors between T2w MR and PET images were found in one patient and moderate misalignment errors in five patients (Fig. 7c) compared to no major and only two moderate misalignment errors for the proposed free-breathing approach. One patient was excluded from this evaluation, because the patient had large pleural effusion which led to artefacts during the tissue segmentation process required for the AC calculation.

Improvement in PET Image Quality

The improvement in PET image quality using MCIR with MR-based MVF is shown for large and small uptake structures in Fig. 8. Respiratory motion leads to blurring of the uptake in the myocardium (Fig. 8a). MCIR compensated for this blurring effect and improved visualization and quantification. The profile of a cross-section of the urethra demonstrated the blurring effect of respiration on small uptake structures and how MCIR could restore uptake profiles, leading to higher uptake values compared to both the uncorrected and 30%-gated PET images (Fig. 8b).

Over all 33 features assessed in the 11 patients, the uncorrected PET reconstruction led to an average FWHM value which was 20 $\pm$ 40 % ($p = 0.005$) larger than the 30%-gated PET reconstruction. The difference between MCIR and 30%-gated PET images was not significant (3 $\pm$ 21 % with $p>0.5$). The SNR measured in the MCIR images was 75 $\pm$ 94 % ($p = 0.004$) higher than in the uncorrected PET images. The 30%-gated PET images also showed an increase in SNR of 51 $\pm$ 91 % ($p > 0.1$) but it was not significant.

DISCUSSION

Respiratory motion amplitudes and breathing patterns varied strongly between patients, an observation previously highlighted by other studies (45). The proposed approach provided accurate motion information and a highly efficient PET-MR examination for all patients. No breathhold instructions were required which ensured high patient comfort. Acquiring 3D high-resolution T1w and T2w MR images using respiratory gating in these patients would have unnecessarily doubled the PET-MR scan time even for a gating acceptance window of 5 mm which is more than three times larger than the spatial resolution. Gated MR scans would not have provided motion information to improve the PET image quality.

The improvement of MR and PET image quality achieved with MCIR depends on patients' respiratory amplitude and breathing pattern which can even vary within one examination. The uncorrected and MCIR T1w images displayed in Fig. 4b show only subtle differences. Spending additional scan time on obtaining respiratory motion information might therefore add little to no additional diagnostic benefit. The uncorrected T2w images on the other hand show large artefacts at the interface between spleen and lung, which are successfully corrected for using MCIR. The proposed acquisition using GRPE provided 3D high-resolution respiratory motion information without an increase in scan time and ensured high image qualities for all patients in a highly efficient way avoiding unnecessarily lengthy scan times.

Respiratory motion correction approaches have been proposed previously for PET-MR. Nevertheless, the majority of these approaches require additional scan time to obtain MVFs reducing the overall efficiency of the PET-MR scan (12–18). In addition, motion information is commonly not acquired with high isotropic

resolution limiting the accuracy of MVFs. In PET-MR patient studies of the thorax or abdomen, previously published MCIR methods achieved an improvement in SNR between 20 and 30% (12–14,18) and up to 50% (13). Manber et al. reported in increase in average SUV of high uptake regions of 20% (17). Improvements in FWHM using MCIR were only assessed for a few methods and range from less than 10% (16) to 60% (14). Our improvements of SNR and FWHM using MCIR were in agreement with these previous findings.

PET MCIR achieved a similar resolution (FWHM) as the 30%-gated PET reconstruction but ensured higher SNR than the gating approach. Compared to the uncorrected PET reconstruction, respiratory gating led to higher maximum uptake values (as shown in the profiles in Fig. 8) but also an increased standard deviation of the background signal, because fewer counts were used for the image reconstruction. Depending on the patient, one of the two effects dominated, leading to SNR increases or decreases and a not statistically significant difference in SNR between 30%-gated and uncorrected PET reconstruction. MCIR on the other hand achieved higher maximum uptake values without an increase in background noise leading to a significant improvement in SNR. This improvement in SNR could be utilized to reduce the dose of the injected PET tracer. Figure 9 compares PET images using all the data (standard dose) and using only 25% of the data (reduced dose). For the standard dose small structures such as the healthy tissue surrounding a kidney cyst are clearly visible for the 30%-gated PET and the MCIR images. Nevertheless, for the reduced dose the SNR in the 30%-gated PET images is not sufficient to clearly depict this small anatomical feature. One limitation of this study is the small number of patients. Further patient studies focusing on a specific pathology are required to fully evaluate the impact the proposed approach could have on diagnostic accuracy and reproducibility.

The binning of MR and PET data was carried out based on a respiratory belt signal which provided a global motion surrogate with excellent temporal resolution. Although respiratory belts do not directly measure the most dominant respiratory motion component of the abdomen (i.e. foot-head translation), we found good correlation between the self-navigator signals describing foot-head signal variations and the respiratory belts. This is also confirmed by recent studies which have shown that respiratory belts yield very robust respiratory motion information (10,46). In addition, we only used the respiratory belt to bin the acquired data. Quantitative displacement metrics are then obtained through the image registration of the respiratory-resolved 3D MR images. In contrast to a standard MR pencil-beam navigator, this displacement information is available for each pixel. Self-navigator signals can be obtained from GRPE data (8) but due to the long TR of the T2w MR scan, the temporal resolution of the self-navigator signal

was not be sufficient for the binning of the PET data acquired during the T2w scan. Additional self-navigator information (i.e. $k_y = k_z = 0$ GRPE lines) could be recorded between each TSE train to overcome this limitation. In addition, a self-navigator signal could also be obtained from the PET data (17).

In this study we obtained T1w and T2w MR images using a motion-compensated GRPE approach. The proposed T1w GRE scan could also be extended to post-contrast or even to a dynamic acquisition (27) in order to further improve the diagnostic quality of the PET-MR acquisition (4). Also diffusion-weighted GRPE acquisition would be possible to improve tumor detection and characterization (21), but so far the benefit of diffusion-weighted images for PET-MR applications is still an open research question (47,48). The fat image obtained from the T1w Dixon scan was only used to calculate AC maps. The 3D high-resolution fat image could also provide further diagnostic information such as differentiation and characterization of renal masses based on the absence or presence of fat (5,6).

One limitation of all MR-based AC maps is the smaller FOV of MR compared to PET. This leads to incomplete or distorted visualization of most subjects' arms. Maximum Likelihood reconstruction of Attenuation and Activity algorithms have been suggested to retrieve missing AC information (49). In addition, bone and air are challenging to distinguish in MR but have very different AC values. Nevertheless, in the abdomen misclassifying bone as soft tissue leads to small SUV errors below 10%. Atlas based methods could be used to reduces these errors even further (50). Extensions to MR-based AC like (44) including bone segmentation from Dixon input images could easily be adapted and included into the presented GRPE acquisition.

The AC map obtained from the MCIR T1w Dixon scan was compared to the standard breathhold AC map. Although the Dice coefficient showed good agreement between the two maps, the breathhold AC map is not a reliable reference. Artefacts due to incomplete breathholds or attenuation-emission mismatch can impair the AC values in the lungs, which is a possible explanation for the decreased value and high standard deviation of the Dice coefficient for air inside the body. In addition, the air inside the body also includes air in the bowels which can change between the two scans.

Depending on the weight of patients, the TR of the T2w TSE acquisition had to be increased due to specific absorption rate (SAR) limitations which led to increased scan times. Another possibility to reduce SAR without lengthening the scan time would have been to decrease the length of the TSE by using a higher partial Fourier factor.

In this study AC maps were calculated from the multi-echo T1w scan, because these images are similar to the MR images used to get AC information in clinical practice. Nevertheless, fat and water images could

also be obtained from a multi-echo T2w TSE acquisition and a standard fat-suppression pulse could be used for the T1w scan. This would reduce the SAR burden of the TSE scan and allow for shorter TRs and shorten the T1w scan leading to an even faster and more efficient PET-MR examination.

CONCLUSION

We have presented a novel motion-compensated abdominal PET-MR approach providing 3D high-resolution T1w and T2w images and metabolic PET information in a free-breathing PET-MR scan which utilizes all the acquired data leading to a 100% scan efficiency. The MCIR image reconstruction ensures that all image data are in the same motion state and therefore fully spatially aligned. The required respiratory motion information and respiratory-resolved AC maps are obtained from the anatomical MR scans without an increase in scan time. The proposed approach is fast, efficient and comprehensive and could be an important stepping stone to bring simultaneous PET-MR into clinical practice.

ACKNOWLEDGEMENT

This work was part of the SUBLIMA project (http://www.sublima-pet-mr.eu/) supported by the European Union under the seventh framework program (no: 241711). This research was supported by the National Institute for Health Research (NIHR) Biomedical Research Centre at Guy's and St Thomas' NHS Foundation Trust and King's College London. The views expressed are those of the authors and not necessarily those of the NHS, the NIHR or the Department of Health. The PET image reconstruction used for this project was in part developed during the Computational Collaborative Project in Synergistic PET-MR Reconstruction, UK EPSRC grant EP/M022587/1. The authors would also like to thank James Stirling and Sami Jeljeli for their help with the patient scanning and Dr. Christian Kelly-Morland for his help with image assessment.

CITATIONS

1. Judenhofer MS, Wehrl HF, Newport DF, et al. Simultaneous PET-MRI: a new approach for functional and morphological imaging. Nat. Med. [Internet] 2008;14:459–465. doi: 10.1038/nm1700.

2. Gaa J, Rummeny E, Seemann M. Whole-body imaging with PET/MRI. Eur. J. Med. Res. 2004;9:309–312.

3. Antoch G. Whole-Body Dual-Modality PET/CT and Whole-Body MRI for Tumor Staging in Oncology. JAMA [Internet] 2003;290:3199. doi: 10.1001/jama.290.24.3199.

4. Reiner CS, Stolzmann P, Husmann L, Burger IA, H??llner MW, Schaefer NG, Schneider PM, Von Schulthess GK, Veit-Haibach P. Protocol requirements and diagnostic value of PET/MR imaging for liver metastasis detection. Eur. J. Nucl. Med. Mol. Imaging 2014;41:649–658. doi: 10.1007/s00259-013-2654-x.

5. Pedrosa I, Sun MR, Spencer M, Genega EM, Olumi AF, Dewolf WC, Rofsky NM. MR imaging of renal masses: correlation with findings at surgery and pathologic analysis. Radiographics [Internet] 2008;28:985–1003. doi: 10.1148/rg.284065018.

6. Pallwein-Prettner L, Flöry D, Rotter CR, Pogner K, Syré G, Fellner C, Frauscher F, Aigner F, Krause FS, Fellner F. Assessment and characterisation of common renal masses with CT and MRI. Insights Imaging 2011;2:543–556. doi: 10.1007/s13244-011-0116-1.

7. Sotoudeh H, Sharma A, Fowler KJ, McConathy J, Dehdashti F. Clinical application of PET/MRI in oncology. J. Magn. Reson. Imaging [Internet] 2016:n/a-n/a. doi: 10.1002/jmri.25161.

8. Buerger C, Prieto C, Schaeffter T. Highly efficient 3D motion-compensated abdomen MRI from undersampled golden-RPE acquisitions. Magma Magn. Reson. Mater. Physics, Biol. Med. [Internet] 2013;26:419–29. doi: 10.1007/s10334-013-0370-y.

9. Cheng JY, Alley MT, Cunningham CH, Vasanawala SS, Pauly JM, Lustig M. Nonrigid motion correction in 3D using autofocusing with localized linear translations. Magn. Reson. Med. [Internet] 2012;68:1785–97. doi: 10.1002/mrm.24189.

10. Hope TA, Verdin EF, Bergsland EK, Ohliger MA, Corvera CU, Nakakura EK. Correcting for respiratory motion in liver PET/MRI: preliminary evaluation of the utility of bellows and navigated hepatobiliary phase imaging. EJNMMI Phys. [Internet] 2015;2:21. doi: 10.1186/s40658-015-0125-0.

11. Catana C. Motion Correction Options in PET/MRI. Semin. Nucl. Med. [Internet] 2015;45:212–223. doi: 10.1053/j.semnuclmed.2015.01.001.

12. Würslin C, Schmidt H, Martirosian P, Brendle C, Boss A, Schwenzer NF, Stegger L. Respiratory motion

correction in oncologic PET using T1-weighted MR imaging on a simultaneous whole-body PET/MR system. J. Nucl. Med. [Internet] 2013;54:464–71. doi: 10.2967/jnumed.112.105296.
13. Fayad H, Odille F, Schmidt H, Würslin C, Küstner T, Feblinger J, Visvikis D. The use of a generalized reconstruction by inversion of coupled systems (GRICS) approach for generic respiratory motion correction in PET/MR imaging. Phys. Med. Biol. [Internet] 2015;60:2529–46. doi: 10.1088/0031-9155/60/6/2529.
14. Fayad H, Schmidt H, Wurslin C, Visvikis D. Reconstruction incorporated respiratory motion correction in clinical simultaneous PET/MR imaging for oncology applications. J. Nucl. Med. [Internet] 2015;56:884–890. doi: 10.2967/jnumed.114.153007.
15. Furst S, Grimm R, Hong I, Souvatzoglou M, Casey ME, Schwaiger M, Nekolla SG, Ziegler SI. Motion Correction Strategies for Integrated PET/MR. J. Nucl. Med. [Internet] 2015;56:261–269. doi: 10.2967/jnumed.114.146787.
16. Grimm R, Fürst S, Souvatzoglou M, et al. Self-gated MRI motion modeling for respiratory motion compensation in integrated PET/MRI. Med. Image Anal. [Internet] 2015;19:110–120. doi: 10.1016/j.media.2014.08.003.
17. Manber R, Thielemans K, Hutton BF, Barnes A, Ourselin S, Arridge S, O'Meara C, Wan S, Atkinson D. Practical PET Respiratory Motion Correction in Clinical PET/MR. J. Nucl. Med. [Internet] 2015;56:890–896. doi: 10.2967/jnumed.114.151779.
18. Rank CM, Heußer T, Wetscherek A, Freitag MT, Sedlaczek O, Schlemmer H, Kachelrieß M. Respiratory motion compensation for simultaneous PET/MR based on highly undersampled MR data. Med. Phys. [Internet] 2016;43:6234–6245. doi: 10.1118/1.4966128.
19. Martinez-Möller A, Souvatzoglou M, Delso G, Bundschuh RA, Chefd'hotel C, Ziegler SI, Navab N, Schwaiger M, Nekolla SG. Tissue classification as a potential approach for attenuation correction in whole-body PET/MRI: evaluation with PET/CT data. J. Nucl. Med. [Internet] 2009;50:520–526. doi: 10.2967/jnumed.108.054726.
20. Sureshbabu W, Mawlawi O. PET/CT imaging artifacts. J. Nucl. Med. Technol. [Internet] 2005;33:156-61–4.
21. Martinez-Moller A, Eiber M, Nekolla SG, Souvatzoglou M, Drzezga A, Ziegler S, Rummeny EJ, Schwaiger M, Beer a. J. Workflow and Scan Protocol Considerations for Integrated Whole-Body PET/MRI in Oncology. J. Nucl. Med. [Internet] 2012;53:1415–1426. doi: 10.2967/jnumed.112.109348.
22. Seung SL, Jae HB, Hong HS, Seong HP, Hyung JW, Yong MS, Lee MG. Image quality and focal lesion

detection on T2-weighted MR imaging of the liver: Comparison of two high-resolution free-breathing imaging techniques with two breath-hold imaging techniques. J. Magn. Reson. Imaging 2007;26:323–330. doi: 10.1002/jmri.21002.
23. Batchelor PG, Atkinson D, Irarrazaval P, Hill DLG, Hajnal J, Larkman D. Matrix description of general motion correction applied to multishot images. Magn. Reson. Med. [Internet] 2005;54:1273–80. doi: 10.1002/mrm.20656.
24. Lamare F, Ledesma Carbayo MJ, Cresson T, Kontaxakis G, Santos a, Le Rest CC, Reader AJ, Visvikis D. List-mode-based reconstruction for respiratory motion correction in PET using non-rigid body transformations. Phys Med Biol [Internet] 2007;52:5187–5204. doi: 10.1088/0031-9155/52/17/006.
25. Tsoumpas C, Mackewn JE, Halsted P, King AP, Buerger C, Totman JJ, Schaeffter T, Marsden PK. Simultaneous PET-MR acquisition and MR-derived motion fields for correction of non-rigid motion in PET. Ann Nucl Med [Internet] 2010;24:745–750. doi: 10.1007/s12149-010-0418-2.
26. Boubertakh R, Prieto C, Batchelor PG, Uribe S, Atkinson D, Eggers H, Sørensen TS, Hansen MS, Razavi RS, Schaeffter T. Whole-heart imaging using undersampled radial phase encoding (RPE) and iterative sensitivity encoding (SENSE) reconstruction. Magn. Reson. Med. [Internet] 2009;62:1331–7. doi: 10.1002/mrm.22102.
27. Prieto C, Uribe S, Razavi R, Atkinson D, Schaeffter T. 3D Undersampled Golden-Radial Phase Encoding for DCE-MRA Using Inherently Regularized Iterative SENSE. Magn. Reson. Med. 2010;64:514–526.
28. Lu W, Yu H, Shimakawa A, Alley M, Reeder SB, Hargreaves BA. Water-fat separation with bipolar multiecho sequences. Magn. Reson. Med. 2008;60:198–209. doi: 10.1002/mrm.21583.
29. Kolbitsch C, Prieto C, Smink J, Schaeffter T. Highly efficient whole-heart imaging using radial phase encoding-phase ordering with automatic window selection. Magn. Reson. Med. [Internet] 2011;66:1008–18. doi: 10.1002/mrm.22888.
30. Johnson KM, Block WF, Reeder SB, Samsonov A. Improved least squares MR image reconstruction using estimates of k-space data consistency. Magn. Reson. Med. [Internet] 2012;67:1600–1608. doi: 10.1002/mrm.23144.
31. Cruz G, Atkinson D, Buerger C, Schaeffter T, Prieto C. Accelerated motion corrected three-dimensional abdominal MRI using total variation regularized SENSE reconstruction. Magn. Reson. Med. [Internet] 2016;75:1484–1498. doi: 10.1002/mrm.25708.
32. Rueckert D, Sonoda LI, Hayes C, Hill DL, Leach MO, Hawkes DJ. Nonrigid registration using free-form deformations: application to breast MR images. IEEE Trans. Med. Imaging [Internet] 1999;18:712–21.

doi: 10.1109/42.796284.
33. Berglund J, Kullberg J. Three-dimensional water/fat separation and T 2 * estimation based on whole-image optimization-Application in breathhold liver imaging at 1.5 T. Magn. Reson. Med. 2012;67:1684–1693. doi: 10.1002/mrm.23185.
34. Qiao F, Pan T, Clark Jr JW, Mawlawi OR. A motion-incorporated reconstruction method for gated PET studies. Phys Med Biol [Internet] 2006;51:3769–3783. doi: 10.1088/0031-9155/51/15/012.
35. Dey J. Reconstruction Algorithms for Motion Correction in Emission. IEEE Trans Nucl Sci. 2010;56:2739–2749.
36. Tsoumpas C, Aguiar P, Nikita KS, Ros D, Thielemans K. Evaluation of the single scatter simulation algorithm implemented in the {STIR} library. In: Nuclear Science Symposium Conference Record, 2004 IEEE. Vol. 6. ; 2004. p. 3361–3365 Vol. 6. doi: 10.1109/NSSMIC.2004.1466455.
37. Polycarpou I, Thielemans K, Manjeshwar R, Aguiar P, Marsden PK, Tsoumpas C. Comparative evaluation of scatter correction in {3D PET} using different scatter-level approximations. Ann Nucl Med [Internet] 2011;25:643–649. doi: 10.1007/s12149-011-0514-y.
38. Pruessmann KP, Weiger M, Boernert P, Boesiger P. Advances in sensitivity encoding with arbitrary k-space trajectories. Magn. Reson. Med. 2001;46:638–651.
39. Thielemans K, Tsoumpas C, Mustafovic S, Beisel T, Aguiar P, Dikaios N, Jacobson MW. STIR: software for tomographic image reconstruction release 2. Phys Med Biol [Internet] 2012;57:867–883. doi: 10.1088/0031-9155/57/4/867.
40. Buerger C, Clough RE, King a P, Schaeffter T, Prieto C. Nonrigid motion modeling of the liver from 3-D undersampled self-gated golden-radial phase encoded MRI. IEEE Trans. Med. Imaging [Internet] 2012;31:805–15. doi: 10.1109/TMI.2011.2181997.
41. Botnar RM, Stuber M, Danias PG, Kissinger K V, Manning WJ. Improved coronary artery definition with T2-weighted, free-breathing, three-dimensional coronary MRA. Circulation [Internet] 1999;99:3139–48.
42. Piccini D, Monney P, Sierro C, et al. Respiratory self-navigated postcontrast whole-heart coronary MR angiography: initial experience in patients. Radiology [Internet] 2014;270:378–86. doi: 10.1148/radiol.13132045.
43. Pang J, Bhat H, Sharif B, Fan Z, Thomson LEJ, Labounty T, Friedman JD, Min J, Berman DS, Li D. Whole-heart coronary MRA with 100% respiratory gating efficiency: Self-navigated three-dimensional retrospective image-based motion correction (TRIM). Magn. Reson. Imaging [Internet] 2014;71:67–74.

doi: 10.1002/mrm.24628.
44. Dice LR. Measures of the Amount of Ecologic Association Between Species. Ecology [Internet] 1945;26:297–302. doi: 10.2307/1932409.
45. Kolbitsch C, Prieto C, Buerger C, Harrison J, Razavi R, Smink J, Schaeffter T. Prospective high-resolution respiratory-resolved whole-heart MRI for image-guided cardiovascular interventions. Magn. Reson. Med. [Internet] 2012;68:205–13. doi: 10.1002/mrm.23216.
46. Santelli C, Nezafat R, Goddu B, Manning WJ, Smink J, Kozerke S, Peters DC. Respiratory bellows revisited for motion compensation: Preliminary experience for cardiovascular MR. Magn. Reson. Med. [Internet] 2011;65:1097–1102. doi: 10.1002/mrm.22687.
47. Buchbender C, Hartung-Knemeyer V, Beiderwellen K, Heusch P, Kühl H, Lauenstein TC, Forsting M, Antoch G, Heusner TA. Diffusion-weighted imaging as part of hybrid PET/MRI protocols for whole-body cancer staging: Does it benefit lesion detection? Eur. J. Radiol. [Internet] 2013;82:877–882. doi: 10.1016/j.ejrad.2013.01.019.
48. Morani AC, Elsayes KM, Liu PS, Weadock WJ, Szklaruk J, Dillman JR, Khan A, Chenevert TL, Hussain HK. Abdominal applications of diffusion-weighted magnetic resonance imaging: Where do we stand. World J. Radiol. [Internet] 2013;5:68–80. doi: 10.4329/wjr.v5.i3.68.
49. Vandenberghe S, Marsden PK. PET-MRI: a review of challenges and solutions in the development of integrated multimodality imaging. Phys Med Biol [Internet] 2015;60:R115–R154. doi: 10.1088/0031-9155/60/4/R115.
50. Hofmann M, Bezrukov I, Mantlik F, Aschoff P, Steinke F, Beyer T, Pichler BJ, Schölkopf B. MRI-Based Attenuation Correction for Whole-Body PET/MRI: Quantitative Evaluation of Segmentation- and Atlas-Based Methods. J. Nucl. Med. [Internet] 2011;52:1392–1399. doi: 10.2967/jnumed.110.078949.

Table 1: MR Acquisition parameters. SPAIR Spectral Attenuated Inversion Recovery.

	Multi-Echo T1w GRE	**T2w TSE**
TE (ms) / ΔTE (ms)	1.29 / 1.90	201
TR (ms)	7.3	2000
Flip angle (degrees)	12	90/120
FOV FH x AP x RL (mm^3)	288 x 519 x 519	288 x 519 x 519
Resolution (mm^3)	1.5 x 1.5 x 1.5	1.5 x 1.5 x 1.5
Acquisition matrix	148 x 192 x 192	192 x 163 x 144
Partial echo factor	0.77	1
Partial Fourier factor	1	0.85
Fat saturation	Dixon	SPAIR
Acquisition time	4min 30s	4min 50s

Figure 1: Comparison of the standard and proposed approach for abdominal PET-MR. For the standard PET-MR approach MR images are obtained during multiple breathholds or using respiratory triggering. To ensure MR does not exceed PET scan times, images with only low through-plane resolution can be acquired and need to be repeated in different scan orientations (e.g. coronal and axial TSE scans). The proposed approach obtains 3D multi-echo GRE and fat-saturated TSE acquisitions with high isotropic resolution (1.5 mm^3) and PET scans during free-breathing. Motion-compensated image reconstruction (MCIR) is used to minimize respiratory motion artefacts (white arrows) and to ensure all MR and PET images are fully spatially aligned. Dynamic attenuation maps (mu maps) and non-rigid respiratory motion information are obtained directly from the anatomical MR scans without an increase in scan time.

Figure 2: Golden Radial Phase Encoding (GRPE). (a,b) A respiratory surrogate is used to assign each acquired GRPE line ($1…N_A$) to a respiratory motion state. **(c)** The acquired GRPE data is binned into N_{Resp} respiratory bins and motion information is obtained with a non-rigid image registration algorithm. **(d)** In the final motion-compensated image reconstruction (MCIR) all the acquired GRPE data is used together with the non-rigid motion information to obtain a motion-corrected image.

Figure 3: Accuracy of motion estimation. (a) Example of locations of landmark points for one patient. Two points were selected in the liver (L), three in the right kidney (RK) and three in the left kidney (LK). **(b)** Maximum displacement of landmark points (D_{max}) during the respiratory cycle (squares) and average target-registration-error (TRE, circles) for each patient. Average value and standard deviation of D_{max} and TRE are also given (colored crosses) for T1w (blue) and T2w images (green).

Figure 4:MR image quality. Comparison of uncorrected (Uncorr) and motion-compensated (MCIR) T1w water **(a-c)** and T2w images **(d-f)** MR images. (a,e) 62-year-old male patient imaged for melanoma staging. (b) 65-year-old male patient with a metastatic neuroendocrine tumor. (c,f) 51-year-old female lymphoma patient. (d) 59-year-old male patient with sarcoidosis and kidney cysts. The proposed MCIR approach improves the visualization of cysts (a,b,d,e) and vessel structures (c,f). Cysts commonly appear bright on T2w and dark on T1w images (d,b,e). The patient in (a) has got hemorrhagic cysts in the kidney which appear bright on T1w images. The FOV of all images was reduced from the original 288 x 519 x 519 mm^3 to enhance visualization of anatomical and pathological image features.

Figure 5: Improvement in feature sharpness (FS) using MCIR. (a) FS was calculated along the right diaphragm (RD), the right kidney (RK) and left kidney (LK). **(b)** Example of a line plot perpendicular to the right diaphragm and the increase in FS using MCIR compared to the uncorrected images (Uncorr). **(c)** Relative improvement of FS using MCIR compared to the uncorrected images for T1w (blue bars) and T2w (green bars) images.

Figure 6: Accuracy of attenuation correction (AC) map. Fat and water images, tissue segmentation (Segm) and attenuation correction (AC) maps calculated from the standard end-expiratory breathhold acquisition and the proposed free-breathing MCIR T1w scan. The free-breathing scan yields an AC map for each respiratory phase and here the end-expiratory image is shown as it is most similar to the breathhold scan. Segmentation artefacts (black arrows) and fat-water swap (white arrow) are visible in the breathhold AC image. The Dice similarity coefficient was calculated between the two tissue segmentations and showed good agreement over all patients.

Figure 7: Artefacts due to inaccuracies in the AC map. (a) An incomplete breathhold during the acquisition of the standard AC map led to artefacts in the MR water images (white arrow) and AC map (black arrow) and created a false uptake region in the lungs in the PET images (white arrow). The proposed free-breathing approach did not show such artefacts. **(b)** A deep breathhold caused a strong deformation of the liver in the standard breathhold AC map which did not match the shape of the liver during the free-breathing PET acquisition. This led to a signal drop in large areas (black arrows), which was scored as major misalignment errors. The propose approach obtained the AC information during free-breathing and ensured accurate alignment between AC map and PET data (scored with minor misalignment errors). (c) Score of misalignment errors between PET and T2w MR images for the standard breathhold (BH) and proposed free-breathing approach.

Figure 8: Improvement of PET image quality using MCIR. Overlay of MCIR PET images onto MCIR T2w MR images, zooms for uncorrected, 30% gated and MCIR PET images and line profiles. **(a)** 51-year-old male patient with lymphoma. **(b)** 47-year-old male patient with lymphoma. Both patients were imaged with ^{18}F-FDG.

Figure 9: Improvement in SNR using MCIR. 59-year-old male patient with sarcoidosis and kidney cysts. The hypo-intense kidney cyst is clearly visible in the MCIR T1w water image (*). The uptake in the thin healthy kidney tissue surrounding the cyst (white arrow heads) can be seen in the 30% gated and MCIR PET image equally well assuming a standard injection dose of the PET tracer (100%). A simulated dose reduction to 25% leads to low SNR in the gated PET image and strongly impairs the visibility of this structure. MCIR utilizes all the available data and therefore leads to higher SNR and better image quality.